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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/032,592 | 10/24/2001 | Firdous Farooqui | 2065-181 | 8167 |

22471 7590 08/23/2004

PATENT LEGAL DEPARTMENT/A-42-C
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EXAMINER

CEPERLEY, MARY

ART UNIT PAPER NUMBER

1641

DATE MAILED: 08/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|--------------------------|---------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/032,592 | FIRDOUS ET AL | |
| | Examiner | Art Unit | |
| | Mary (Molly) E. Ceperley | 1641 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 February 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-74 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-74 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>1/31/2002</u> | 6) <input type="checkbox"/> Other: _____ |

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1) The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2) The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3) Claims 1, 11-16, 20, 29 and 36 are rejected under 35 U.S.C. 102(e) as anticipated by Chait et al (US 2003/0045694 A1). At col. 91, paragraph [1290] Chait et al describe a method for preparing a protein-oligonucleotide conjugate in which an oligonucleotide containing a reactive amine group is reacted with a heterobifunctional cross-linking reagent to form an activated oligonucleotide-heterofunctional linker conjugate [corresponds to step (A) of instant claim 1], the protein is reacted with 2-iminothiolane to introduce a reactive sulfhydryl group into the protein (i.e. the protein is "thiolated") and the thiol-containing protein is then reacted with the activated oligonucleotide to form a covalent protein-oligonucleotide conjugate [corresponds to step (B) of instant claim 1]. The method of the reference comprises the same steps as, and therefore anticipates, the method of instant claim 1. The product produced by the process of Chait et al anticipates the product of instant claim 29 which is prepared using the same method steps.

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For the limitations of instant claim 11 "wherein said second group of said heterofunctional linker is a maleimide group" and claims 12 and 13, see Chait et al, paragraph [1290] wherein SULFO-SMCC {N-sulfosuccinimidyl 4-(N-maleimidomethyl)cyclohexane-1-carboxylate} is used as a heterobifunctional cross-linking agent.

For the limitations of claims 14-16, directed to the formation of the thiolated protein using an imiothiolane moiety, see the Chait et al method of paragraph [1290] which uses 2-iminothiolane as a reactant to thiolate a protein.

For the limitations of claims 20 and 36, "wherein said protein is a hapten", see paragraph [1290] of Chait et al which discusses "the capacity of the protein to associate with its cognate antibody"; this statement regarding the ability of the protein to associate with an antibody indicates that the protein is a hapten.

4) Claims 2-28 and 30-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chait et al (US 2003/0045694 A1) taken in view of Reddy et al (U.S. 5,648,213).

Chait et al is applied for the reasons stated in paragraph **3)** above.

Reddy et al is applied for the reasons stated in paragraph **5)**, first subparagraph, of the February 18, 2004 Office action, i.e. its description of the formation of an oligonucleotide-protein conjugate by the method of the instant invention with the sole difference being that the reactive thiol group of the protein used in Reddy et al is a native thiol group while the thiol group of the protein used in the instant invention is an added thiol group. Reddy et al is further applied for its description of parameters which are routinely modified in the art as set forth in paragraph **5)**, second subparagraph, of the February 18, 2004 Office action.

The instant claims are rendered obvious by the basic method set forth in Chait et al described above taken in view of the description of Reddy et al which establishes the level of skill in the art with regard to routine process modifications. The features of the dependent claims are either specifically described by the references or constitute obvious variations in parameters which are routinely modified in

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the art (e.g. choice of well known equivalent analytes and heterobifunctional linkers) and which have not been described as critical to the practice of the invention. For example, for the use of a 5'NH₂ oligonucleotide (instant claim 5), see Reddy et al, col. 18, line 50; for the use of a sulfo-SMCC hetero bifunctional linker (instant claim 12), see both Reddy et al, col. 19, lines 18-25 and Chait et al, paragraph [1290]; for an immunoglobulin (protein) specific for a drug (instant claim 22), see Reddy et al, Example 12; for well known equivalent heterobifunctional linkers (instant claim 12), see Reddy et al, col. 6, line 8 – col. 7, line 13.

5) Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.


6) Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary (Molly) E. Ceperley whose telephone number is (571) 272-0813. The examiner can normally be reached from 8 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le, can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

August 20, 2004


Mary (Molly) E. Ceperley
Primary Examiner
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